



# Young Zanzibari Children with Iron Deficiency, Iron Deficiency Anemia, Stunting, or Malaria Have Lower Motor Activity Scores and Spend Less Time in Locomotion<sup>1–3</sup>

Deanna K. Olney,<sup>4\*</sup> Ernesto Pollitt,<sup>4</sup> Patricia K. Kariger,<sup>5</sup> Sabra S. Khalfan,<sup>6</sup> Nadra S. Ali,<sup>6</sup> James M. Tielsch,<sup>7</sup> Sunil Sazawal,<sup>7</sup> Robert Black,<sup>7</sup> Darrell Mast,<sup>7</sup> Lindsay H. Allen,<sup>4,8</sup> and Rebecca J. Stoltzfus<sup>5</sup>

<sup>4</sup>Program in International and Community Nutrition, University of California, Davis, CA 95616; <sup>5</sup>Division of Nutritional Sciences, Cornell University, Ithaca, NY 14853; <sup>6</sup>Pemba Public Health Laboratory-Ivo de Carneri, Zanzibar, United Republic of Tanzania; <sup>7</sup>Bloomberg School of Public Health, The Johns Hopkins University, Baltimore, MD 21205; <sup>8</sup>USDA-Agricultural Research Service-Western Human Nutrition Research Center, Davis, CA 95616

## Abstract

Motor activity improves cognitive and social-emotional development through a child's exploration of his or her physical and social environment. This study assessed anemia, iron deficiency, hemoglobin (Hb), length-for-age Z-score (LAZ), and malaria infection as predictors of motor activity in 771 children aged 5–19 mo. Trained observers conducted 2- to 4-h observations of children's motor activity in and around their homes. Binary logistic regression assessed the predictors of any locomotion. Children who did not locomote during the observation (nonmovers) were excluded from further analyses. Linear regression evaluated the predictors of total motor activity (TMA) and time spent in locomotion for all children who locomoted during the observation combined (movers) and then separately for crawlers and walkers. Iron deficiency (77.0%), anemia (58.9%), malaria infection (33.9%), and stunting (34.6%) were prevalent. Iron deficiency with and without anemia, Hb, LAZ, and malaria infection significantly predicted TMA and locomotion in all movers. Malaria infection significantly predicted less TMA and locomotion in crawlers. In walkers, iron deficiency anemia predicted less activity and locomotion, whereas higher Hb and LAZ significantly predicted more activity and locomotion, even after controlling for attained milestone. Improvements in iron status and growth and prevention or effective treatment of malaria may improve children's motor, cognitive, and social-emotional development either directly or through improvements in motor activity. However, the relative importance of these factors is dependent on motor development, with malaria being important for the younger, less developmentally advanced children and Hb and LAZ becoming important as children begin to attain walking skills. *J. Nutr.* 137: 2756–2762, 2007.

## Introduction

Motor development and motor activity are 2 important and interrelated components of child development (1). Motor development is the acquisition of motor skills such as sitting, crawling, and walking that involve the development of postural control, strength, balance, and perceptual skills. Motor development generally follows a sequential pattern and it is rare for children to regress. Motor activity encompasses the full range of activities that a child is able to do (i.e. sit, stand, walk) and can be quantified as a motor activity score expressed as multiples of the basal metabolic rate. This score is derived from the duration

of time spent in each motor activity multiplied by an estimated energy cost for each activity (2,3). Locomotion represents a specific set of motor activities that involve movement from one place to another and is associated with improved perceptual development and emotional regulation (4).

Nutritional and health factors such as iron deficiency anemia and stunting influence both motor development (5–9) and motor activity (3,10–13) and these in turn influence each other with effects on children's ability to explore the environment and caregiver behavior. Motor activity is highly dependent on motor development. For example, children who have more advanced motor skills, such as walking compared with crawling, have more opportunities to explore their environment and may have a higher motor activity score based solely on developmental level. On the other hand, children who are less active may evoke caregiver responses that restrict movement (e.g. carrying) and are less supportive for practicing already acquired motor skills and attempting new skills, such as walking and running (14). In a

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<sup>3</sup> Supplemental Table 1 is available with the online posting of this paper at [jn.nutrition.org](http://jn.nutrition.org).

\*To whom correspondence should be addressed. E-mail: [dkolney@ucdavis.edu](mailto:dkolney@ucdavis.edu).

study of Costa Rican infants aged 12–23 mo, caregivers and testers made fewer attempts to encourage children with iron deficiency anemia to attempt test items from the psychomotor portion of the Bayley Scales of Infant Development (10,15). Neither the caregivers nor the testers knew the iron status of the children, but nonetheless encouraged the anemic children less, possibly because they were less active or seemed tired or incapable of doing more.

A study of Indonesian children demonstrated that motor development and motor activity are highly correlated until children are 18 mo old (2). In Jamaica, stunted children aged 12–24 mo had lower motor activity scores than nonstunted children. However, 6 mo of nutritional supplementation with or without psychosocial stimulation eliminated this difference in motor activity (3). In the stunted children, activity levels and exploratory behaviors predicted changes in scores on the Griffiths Scales of Mental Development (16) 1 and 2 y after the initial assessment (17).

The relationship between malaria and motor activity in preschool children has not been investigated, although it is well known that malaria is a common cause of morbidity and mortality in areas where it is endemic (18). The effects of cerebral malaria on cognitive and motor development have been reviewed. In one review, 16% of the children who survived cerebral malaria had neurological sequelae (19). Another review found negative relationships between malaria and many areas of child development, i.e. visuo-spatial skills, memory, and language (20). Although the effects of cerebral malaria are devastating, the more prevalent issue for children living in malaria endemic areas is repeated and chronic mild malaria infections. Two studies have addressed the issue of uncomplicated malaria in children <5 y old and later cognitive or school outcomes (21,22). In Sri Lanka, a retrospective cohort study found that the number of uncomplicated malaria attacks between the ages of 1 and 8 y was negatively correlated with language and math scores at age 6–14 y (21). Gambian children aged 5 y old and younger who received malaria chemoprophylaxis for 1–3 consecutive malaria transmission seasons had attained 0.52 more grade levels 14–17 y later than children who received a placebo (22).

The primary objective of this article is to examine the hypothesis that anemia and stunting are associated with motor activity independently of their established relationship with motor development in Zanzibari children aged 5–19 mo (8). The secondary objective is to examine the relationship between malaria infection and motor activity.

## Materials and Methods

**Description of study area.** Pemba is the northernmost island of the Zanzibar archipelago, which is located off the coast of mainland Tanzania. Stunting and anemia are prevalent (8). *Plasmodium falciparum* malaria is holoendemic and transmitted year-round although parasite density tends to be higher during and immediately following the long rains (May to August) (23). In addition, schistosomiasis and hookworm infestation are common (24). Children's diets consist primarily of breast milk, maize porridge, rice, bread, and tea, supplemented with small portions of fruits, vegetables, and meats. The primary economic activities in Pemba are fishing, subsistence agriculture, and the cultivation of cloves for export.

**Study design.** This study is a cross-sectional baseline analysis of the Child Development Substudy (CDS)<sup>9</sup> conducted as part of a randomized placebo-controlled trial of the effects of supplementation with iron (12.5 mg) + folic acid (50 µg), zinc (10 mg), and iron+folic acid+zinc

on morbidity, mortality, and growth in children aged 1–35 mo at baseline (25). The substudy was designed to examine the effects of these supplements on child development in terms of motor development and activity and language and social development. In this article, the baseline associations between motor activity and iron status, length-for-age Z-score (LAZ), and malaria infection are presented. Ethical approval was received from the internal review boards of Johns Hopkins University, the University of California at Davis, Cornell University, and the Ministry of Health, Zanzibar.

**Subjects and enrollment.** All children in Pemba between the ages of 1 and 35 mo were invited to participate in the main trial (25). For the CDS, neighborhoods (both rural and urban) within Wete district, 1 of 4 districts in Pemba, were selected based on geographic convenience. Children aged 5–18 mo at enrollment in the main trial were asked to participate in the CDS. Consent was obtained from the primary caregiver at the time of enrollment into the main trial. Between February and May 2001, 932 children were enrolled in the substudy and completed their baseline assessments.

**Exclusion criteria.** Children who were missing observation data ( $n = 28$ ), milestone assessment ( $n = 46$ ), or clinic assessment ( $n = 37$ ) only, or any combination of these variables ( $n = 50$ ) were excluded from these analyses, resulting in a sample of 771 children. Baseline characteristics including socioeconomic status (SES), sex, and age did not differ between those included in the analyses and those who were not.

**Measures and procedures.** Data collection for the substudy occurred in 3 segments: 2 home visits and a clinic visit. At the first home visit, an observer conducted an interview with the primary caregiver to assess the child's current health status. To exclude the influence of current fever and diarrhea on children's behavior, observers asked the caregivers about the health of their children on both the day before the observation and on the day of the observation. If the child was currently ill (i.e. current fever defined by a positive answer to the question "Does your child have a fever?" plus an additional affirmative answer to either "Is there a burning feeling in the child's body?" and/or "Is the child's body hot?") Diarrhea was defined as  $\geq 4$  loose stools in the past 24 h), the observation was rescheduled for the next week.

On the observation day, an observer visited the home, interviewed the primary caregiver about the child's current health, appetite, and sleep and observed the child for 3–4 h. Following the observation, the observer conducted 2 more interviews about the child's motor and language development and assessed the child's highest attained milestone. These measures were conducted after the observation to avoid changes in caregiver behavior related to any bias or expectations raised during the interviews. In addition, observers completed a comment form that included information about the number and types of caregivers and peers present during the observation, where the observation occurred, and the weather that day.

After the home visits were completed, a health clinic visit was scheduled for a blood draw and anthropometric measures. Of the health clinic visits, 74% occurred within 1 wk of the observation and 95% within 2 wk.

**Motor activity.** Observers aimed to collect at least 3 h of continuous observation of the children in and around their homes. All observations began in the morning and were paused if the child fell asleep and at the halfway point when the observer took a break for at least 30 min. For the purpose of these analyses, 2 h of observation was considered to be complete. Twenty mutually exclusive codes (listed in Supplemental Table 1) were used to record motor activity [adapted from one used by Pollitt et al. in Indonesia (1)]. A specially designed program (Child Activity Observer software) for handheld computers (Visor, Handspring, and Palm M100 and M105) allowed for continuous recording of the children's activities and for the calculation of total and percent time spent in each activity.

Extensive training and standardization of 19 observers was conducted prior to the start of the study using demonstrations, videos, and paired observations. The Child Activity Observer software program provided kappa scores (26) for between-observer comparisons. For every motor code in which at least 15 instances were marked, inter-observer agreement reached at least 90% for all pair-wise comparisons prior to the study.

<sup>9</sup> Abbreviations used: CDS, Child Development Substudy; Hb, hemoglobin; LAZ, length-for-age Z-score; SES, socioeconomic status; TMA, total motor activity; ZPP, zinc protoporphyrin.

We calculated total motor activity (TMA) score as the sum of the products of the percent of time spent in each activity multiplied by the estimated energy cost of each activity (Supplemental Table 1). This method has been used previously in Indonesia (1), India (27), and Jamaica (3) and the estimated energy costs are based on work by Torun et al. (28). Locomotion was defined as the sum of the percent time children spent crawling, walking, and running during the observation. Percent time was used due to the variability in the total observation times (2–4 h).

**Attained milestone.** The highest motor milestone that a child had achieved was recorded following the observation. An observer showed the primary caregiver a picture chart containing 14 gross motor milestones that has been used in Indonesia (2) and is based on the work of McGraw (29). The motor milestones represented by the pictures were explained verbally to the caregiver, following which the observer pointed to each milestone and asked if it had been performed by the child (definitions listed in Supplemental Table 1). The child was then asked to demonstrate the highest reported milestone, which is the variable used in these analyses. Additional information about this measure is available (8).

**Clinical assessments.** Venous blood (3–5 mL) was collected at the clinic and divided into 3 aliquots. Whole blood was used immediately to measure hemoglobin (Hb) (Hemocue) and to prepare thick and thin blood films. The blood films were transported to the laboratory where they were fixed, stained with Giemsa, and examined for malaria parasites. We counted parasites per 200 leukocytes and if none were found, we continued counting up to 500 leukocytes. Parasite density was calculated assuming 8000 leukocytes/ $\mu$ L blood (30). For these analyses, malaria parasite density was divided into 4 categories (0 = 0, 1 = 1–999, 2 = 1000–4999, and 3  $\geq$  5000 parasites/ $\mu$ L blood) and does not necessarily indicate a clinical episode of malaria. Aliquot 2 was used to measure zinc protoporphyrin (ZPP) (hematofluorometer, Aviv Biochemical) and total leukocyte count. Aliquot 3 was transferred into a heparinized, zinc-free polypropylene tube and transported in a cooler to the laboratory where it was centrifuged and stored in a  $-70^{\circ}\text{C}$  freezer for later analyses.

Trained staff measured recumbent length to the nearest 0.1 cm using a wooden length board (Shorr Productions). Three measures were taken and the mean value used in data analysis.

**SES.** The SES variable used in these analyses was a composite score based on parental responses to a questionnaire. The questionnaire included questions about personal and family resources (annual cash income, parental education, and father's employment) and the quality of the home (wall type, floor type, and source of water). For a more detailed discussion of the construction of this variable, see Kariger et al. (8).

**Statistical analyses.** Data were analyzed in SPSS version 13.0. Epi Info 2002 (CDC) was used to calculate LAZ using the WHO 1978 reference charts. Malaria parasite density was highly skewed and was therefore divided into 4 categories (0 = 0, 1 = 1–999, 2 = 1000–4999, and 3  $\geq$  5000 parasites/ $\mu$ L blood) for use in the regression models. These divisions were based on previous work conducted in Zanzibari children 0–5 y old (24).

Study characteristics are presented for all children combined and by motor activity and development groups (nonmovers, crawlers, and walkers). These values are presented as means  $\pm$  SD for continuous variables and  $n$  (%) for categorical variables.

Binary logistic regression was used to assess the predictors of any locomotion (0 = nonmovers, 1 = movers). Nonmovers were defined as children who did not locomote at all during the observation and movers were those who locomoted for at least 0.1% of the observation. SES, sex, age, attained milestone, LAZ score, Hb, malaria infection, and season were considered for inclusion in the model and excluded if they did not significantly contribute to the model ( $P > 0.10$ ). Results are presented as OR, with an OR  $> 1$  representing a higher likelihood of locomoting during the observation. Predictors were considered significant when  $P < 0.05$ . Nonmovers were excluded from additional analyses.

We then used linear regression models to evaluate the predictors of TMA and percent time spent in locomotion. These analyses were first done with all of the children combined and then separately for crawlers and walkers (defined by motor milestone attainment). Crawlers were

children not yet able to walk with assistance and walkers were those able to at least walk with assistance. SES, sex, and age were controlled for in all models. Attained motor milestone, LAZ score, iron status [iron-deficient anemic (Hb  $< 100$  g/L and ZPP  $\geq 90$   $\mu$ mol/mol heme), iron deficient, not anemic (ZPP  $\geq 90$   $\mu$ mol/mol heme), anemic, not iron deficient (Hb  $< 100$  g/L), and normal], malaria infection, and season [dry season and beginning of heavy rain season (February to April) = 0 and end of heavy rain season (May) = 1 (23)] were then entered into the models as predictors of TMA and percent time spent in locomotion. The number of caregivers and peers present, percent time spent inside the house, and whether or not it was raining during the observation were considered for inclusion but did not contribute to any of the models ( $P > 0.10$ ). The interval between the observation and the clinic visit was also considered but did not significantly change any of the relationships between the blood measures and the activity outcomes and was therefore excluded from the analyses.

To examine the relationship between Hb concentration and TMA and locomotion, the iron status variables were replaced with Hb concentration in additional models for both TMA and time spent in locomotion. Other than this replacement, these analyses were conducted in the same way and included the same variables as described above.

The results from the linear regression models with TMA and time spent in locomotion as the outcomes are presented as the regression coefficients and the associated  $P$ -values for each predictor variable. The variables were considered significant predictors if  $P < 0.05$  and marginally significant if  $P < 0.10$ . The  $P$ -values represent a significant linear trend for continuous variables and a significant difference from the reference category for categorical variables.

## Results

**Subject characteristics.** The study subjects were  $\sim 50\%$  male and the proportion of males to females did not differ across the movement groups (nonmovers, crawlers, and walkers; Table 1). The median milestone attained for each of the movement groups was: Sit 2 (sitting without support) for the nonmovement group, Stand 1 (standing with support) for the crawlers, and Walk 2 (walking without support) for the walkers. In this population, iron deficiency (ZPP  $> 90$   $\mu$ mol/mol heme), anemia (Hb  $< 100$  g/L), stunting (LAZ  $< -2.0$ ), and malaria were prevalent. Seventy-seven percent of the children were iron deficient, 58.9% were anemic, and 9.5% were severely anemic. Of the 261 children (33.9%) who tested positive for malaria, 73.9% were anemic and 70.8% were iron-deficient anemic (data not shown).

**Predictors of any locomotion.** Age, Hb, and attained milestone significantly predicted whether or not children locomoted (Table 2). Attained milestone was the strongest predictor of any locomotion. The chance of locomoting during the observation was 65% for children who could creep or crawl, 84% for those who could stand with assistance, 97% for those who could walk with assistance, and 99% for those who could walk alone. Hb concentration was also a significant predictor of whether children locomoted. However, it had little independent influence on whether a child locomoted or not after they had attained the milestone of walking with assistance. A child who had reached this milestone had a 97% chance of locomoting during the observation based on milestone attainment alone. After including age, motor milestone, and Hb in the model, neither malaria infection nor LAZ further predicted whether children locomoted at some point during the observation.

**Predictors of TMA and percent time in locomotion.** Linear regression models were used to assess the predictors of TMA and percent time in locomotion. Analyses were first done with all children who locomoted during the observation in 1 group

**TABLE 1** Characteristics of Zanzibari children aged 5–19 mo by motor activity and development subgroups<sup>1</sup>

	Nonmovers	Crawlers	Walkers	All
<i>n</i>	176	170	425	771
Female	87 (49.4)	82 (48.2)	211 (49.6)	380 (49.3)
Age, mo	7.8 ± 1.9	11.1 ± 2.7	15.0 ± 2.9	12.5 ± 4.0
Hb, g/L	91 ± 17	93 ± 15	96 ± 15	94 ± 16
ZPP <sup>2</sup>	192 ± 138	176 ± 112	180 ± 145	182 ± 137
LAZ	−1.4 ± 1.2	−1.8 ± 1.1	−1.6 ± 1.2	−1.6 ± 1.2
Stunted (LAZ < −2.0)	48 (27.3)	62 (36.5)	157 (36.9)	267 (34.6)
Hb < 100 g/L	112 (63.6)	108 (63.5)	234 (55.1)	454 (58.9)
Iron-deficient anemic <sup>2,3</sup>	98 (60.5)	79 (53.7)	195 (50.3)	372 (53.4)
Malaria parasite density				
0 parasites/μL blood	119 (67.6)	111 (65.3)	280 (65.9)	510 (66.1)
1–999 parasites/μL blood	30 (17.0)	32 (18.8)	97 (22.8)	159 (20.6)
1000–4999 parasites/μL blood	14 (8.0)	15 (8.8)	29 (6.8)	58 (7.5)
≥5000 parasites/μL blood	13 (7.4)	12 (7.1)	19 (4.5)	44 (5.7)

<sup>1</sup> Values are means ± SD or *n* (%).<sup>2</sup> Nonmovers, *n* = 162; crawlers, *n* = 147; walkers, *n* = 388; all children, *n* = 697.<sup>3</sup> Hb < 100 g/L and ZPP ≥ 90 μmol/mol heme.

(movers) and then separately for groups based on attained motor milestone (crawlers and walkers). These analyses were conducted using 2 models, 1 that included iron and anemia status categories (Tables 3 and 4) and 1 that included Hb concentration as a continuous variable (Supplemental Tables 2 and 3). All models controlled for SES, sex, and age and included attained milestone, LAZ, malaria infection, and the season in which the observation was conducted as predictor variables.

**Predictors of TMA.** For all of the children combined, attained milestone, LAZ, iron deficiency with and without anemia, and Hb all significantly predicted TMA after controlling for SES, sex, and age. Malaria infection was marginally associated with TMA. Anemia without iron deficiency and season were not associated with activity in this population (Table 3; Supplemental Table 2). In crawlers, malaria infection significantly predicted lower TMA scores after controlling for sex, age, SES, LAZ score, iron and anemia status or Hb, and season. Hb concentration, iron and anemia status, and LAZ score did not predict TMA scores in this group. In contrast, in walkers, LAZ score, Hb and iron deficiency, and iron deficiency anemia, in addition to attained motor milestone, significantly predicted TMA (Table 3; Supplemental Table 2).

**Predictors of percent time spent in locomotion.** The predictors of percent time spent in locomotion were similar to those for TMA with the exception of season. Children were

significantly more active in terms of locomotion at the end of the heavy rain season (May) as opposed to the dry season and beginning of the heavy rains (February to April). This is likely due to different weather conditions during these 2 seasons, although neither rain nor percent time spent in the house during the observation were significantly associated with percent time spent in locomotion.

For all children combined, higher attained milestone, LAZ scores, and Hb concentrations predicted that children locomoted more during the observation period than those with lower scores. Children with iron deficiency with or without anemia spent less time locomoting compared with those who were not iron deficient. The negative effect of malaria infection on locomotion increased with parasite density (Table 4; Supplemental Table 3). Unadjusted mean differences revealed that children with 1–999 parasites/μL blood spent 12% less time in locomotion, those with 1000–4999 parasites/μL blood spent 42% less time in locomotion, and those with ≥5000 malaria parasites spent ~60% less time in locomotion than children without any parasites. In children in the crawling group, malaria infection, sex (data not shown), and attained milestone significantly predicted time in locomotion (Table 4; Supplemental Table 3). In walkers, LAZ score and Hb were positively associated with time in locomotion, and iron deficiency anemia was negatively associated with locomotion. These significant relationships remained after controlling for SES, sex, age, and attained milestone (Table 4; Supplemental Table 3). Neither malaria infection, sex, nor season was associated with locomotion in this group. Walkers whose Hb was <80 g/L spent 65% less time locomoting than those whose Hb was ≥110 g/L and those who were the most stunted (LAZ < −3.0) spent less than one-half the time locomoting than children whose LAZ was ≥0. There were no differences in the fit of the Hb vs. iron status models for predicting TMA or locomotion in either crawlers or walkers (Tables 3 and 4; Supplemental Tables 2 and 3).

## Discussion

In this sample of Zanzibari children, stunting, anemia, iron deficiency, iron deficiency anemia, and malaria parasitemia were associated with lower TMA as well as less time spent in

**TABLE 2** Predictors of participation in locomotion in 5- to 19-mo-old Zanzibari children<sup>1</sup>

	OR <sup>2,3</sup>	95% CI	P-value
Age, mo	1.32	1.43–1.95	<0.001
Hb, g/L	1.27	1.03–1.57	0.026
Attained milestone	2.24	1.90–2.64	<0.001
Cox and Snell R <sup>2</sup>	0.52		

<sup>1</sup> *n* = 771.<sup>2</sup> Logistic regression was used to evaluate the effects of age, Hb, and attained milestone on whether children locomoted during the observation period (0 = no, 1 = yes).<sup>3</sup> Sex, SES, height-for-age Z-score, malaria infection, and season were considered for inclusion but did not contribute to the model (*P* > 0.10).



**TABLE 3** Multiple regression models of TMA for Zanzibari children aged 5–19 mo and by motor development subgroup<sup>1,2</sup>

Variables	All children, <i>n</i> = 595		Crawlers, <i>n</i> = 170		Walkers, <i>n</i> = 425	
	Coefficient	<i>P</i>	Coefficient	<i>P</i>	Coefficient	<i>P</i>
Motor milestone	0.066	<0.001	−0.004	0.38	0.13	<0.001
LAZ	0.034	<0.001	0.001	0.82	0.29	<0.001
Iron-deficient anemic <sup>3</sup>	−0.071	<0.001	0.011	0.53	−0.064	0.003
Iron-deficient nonanemic	−0.060	0.004	−0.008	0.65	−0.052	0.025
Anemic not iron deficient	−0.001	0.96	0.024	0.29	0.038	0.33
Malaria <sup>4</sup>	−0.014	0.093	−0.013	0.036	−0.004	0.68
Season <sup>5</sup>	0.004	0.82	0.014	0.26	0.004	0.83
<i>R</i> <sup>2</sup>	0.64		0.22		0.64	

<sup>1</sup> Multiple linear regression models with TMA as the dependent variable were conducted separately for each group. All models included SES, gender, and age in addition to the predictor variables listed in the table.

<sup>2</sup> Values are regression coefficients and *P*-value of individual covariates.

<sup>3</sup> Iron-deficient anemic, Hb < 100g/L and ZPP ≥ 90 μmol/mol heme; iron deficient, ZPP ≥ 90 μmol/mol heme; anemic, Hb < 100g/L.

<sup>4</sup> Malaria, parasite density/μL blood categories: 0 = 0, 1 = 1–999, 2 = 1000–4999, 3 ≥ 5000.

<sup>5</sup> Season (month observation conducted): dry season and beginning of heavy rain season (February to April) = 0, end of heavy rain season (May) = 1.

locomotion in children aged 5–19 mo. In crawlers, malaria parasitemia predicted lower TMA and less time spent in locomotion. In walkers, lower LAZ scores and Hb concentrations as well as iron deficiency anemia predicted lower motor activity scores and time spent in locomotion. Hb concentration positively predicted the probability of any locomotion, even after controlling for age and attained motor milestone.

There are other factors that may have also independently influenced TMA or percent time spent in locomotion or attenuated the relationships reported here. These factors include weather, fever, inflammation, illness history, and other stimuli in the environment such as animals. Measures of these variables were not available for these analyses but should be considered in future studies.

In a previous study in Pemba, iron deficiency anemia was causally related to delayed motor and language development measured by a parent report questionnaire (31). In this sample of Zanzibari children, iron deficiency with or without anemia was associated with lower odds of walking alone at baseline (8) and iron+folic acid supplementation with or without zinc reduced the time necessary for children to acquire the skill of walking unassisted (32). Elsewhere, iron deficiency anemia has been

associated with lower scores on global tests of cognitive and psychomotor development (33–37).

This study addresses a related but different outcome; not the effects of LAZ, iron deficiency and anemia, and malaria on motor development, but the effects of these variables on the extent (TMA and duration) and type (locomotion) of motor activity in children who are able to locomote. The few published studies on the relationship between iron deficiency and motor activity were conducted in small samples (11,12) or in a testing situation rather than in the child's natural environment (10). Six-month-old Chilean infants who had iron deficiency anemia had lower spontaneous motor activity scores than their nonanemic peers and the difference in motor activity between iron-deficient anemic and noniron-deficient anemic infants increased at 12 and 18 mo (12). In 12- to 23-mo-old Costa Rican infants, there was a suggestive trend (*P* < 0.10) to lower motor activity in anemic children who had iron deficiency compared with those who were noniron-deficient anemic, as measured by the number of times grid lines were crossed and areas explored during play (10). In 12- and 18-mo-old Indonesian children supplemented with energy and micronutrients including iron, increased Hb

**TABLE 4** Multiple regression models of percent time spent in locomotion for Zanzibari children aged 5–19 mo and by motor development subgroup<sup>1,2</sup>

Variables	All children, <i>n</i> = 595		Crawlers, <i>n</i> = 170		Walkers, <i>n</i> = 425	
	Coefficient	<i>P</i>	Coefficient	<i>P</i>	Coefficient	<i>P</i>
Motor milestone	1.67	<0.001	0.45	0.063	3.21	<0.001
LAZ	0.65	0.003	−0.074	0.80	0.61	0.021
Iron-deficient anemic <sup>3</sup>	−1.81	0.006	0.81	0.38	−1.99	0.012
Iron deficient nonanemic	−1.37	0.054	0.27	0.78	−1.30	0.13
Anemic not iron deficient	−0.49	0.65	1.18	0.32	−0.52	0.72
Malaria <sup>4</sup>	−0.62	0.035	−1.13	<0.001	−0.22	0.56
Season <sup>5</sup>	1.06	0.044	1.72	0.009	0.86	0.18
<i>R</i> <sup>2</sup>	0.39		0.23		0.38	

<sup>1</sup> Multiple linear regression models with percent time locomotion as the dependent variable were conducted separately for each group. All models included SES, gender, and age in addition to the predictor variables listed in the table.

<sup>2</sup> Values are regression coefficients and *P*-value of individual covariates.

<sup>3</sup> Iron-deficient anemic, Hb < 100g/L and ZPP ≥ 90 μmol/mol heme; iron deficient, ZPP ≥ 90 μmol/mol heme; anemic, Hb < 100g/L.

<sup>4</sup> Malaria, parasite density/μL blood categories: 0 = 0, 1 = 1–999, 2 = 1000–4999, 3 ≥ 5000.

<sup>5</sup> Season (month observation conducted): dry season and beginning of heavy rain season (February to April) = 0, end of heavy rain season (May) = 1.

concentration and improved iron stores (represented by decreased erythrocyte protoporphyrin) from baseline to the 6-mo follow-up were positively correlated with higher motor activity scores over the same period (11).

Characteristics of iron deficiency anemia include lethargy and withdrawal in addition to lower oxygen-carrying capacity of the blood. It is possible that the association between iron deficiency with or without anemia and motor activity is due directly to these characteristics. Iron deficiency with and without anemia is associated with lower work performance and endurance in adults and can improve with supplementation (38). However, very little work has been done on this question in children (39–41) and none in preschool children. This association may also be due to tissue iron deficiency resulting in reduced cellular oxidative capacity. These same mechanisms may play a role in the decreased motor activity seen in iron-deficient anemic children. Costa Rican children aged 12–23 mo with iron deficiency anemia were more likely to have abnormal ratings on the endurance portion of the Infant Behavior record of the Bayley Scales of Infant Development (10).

Other mechanisms through which iron deficiency with or without anemia could affect motor activity are alterations in brain myelin and/or neurotransmitter function (42). Iron deficiency alters myelin composition, which may impair the speed at which information is processed. In 4-y-old Chilean children, iron deficiency anemia in infancy was related to longer latencies in auditory brainstem responses and visual evoked potentials (43).

In crawlers, malaria parasitemia was significantly related to TMA as well as time spent in locomotion, although neither Hb concentration nor length was associated with motor activity in this group. Malaria infection could affect motor activity by causing anemia, but anemia was not significantly related to TMA or percent time spent in locomotion in this sample. The results suggest that the direct effects of inflammation, poor appetite, lethargy, and other symptoms secondary to malarial infection, albeit largely asymptomatic subclinical infection, reduced TMA and time spent in locomotion.

Few studies have examined the influence of malaria on motor development, cognitive development, or motor activity in infants and young children. Recent reviews of this question, which concentrated on children older than 5 y (19,20), revealed that the effects of malaria infection in relation to iron status and inflammation change with age, most likely due to repeated infections (24,44). For example, in Zanzibari children, malaria parasitemia was associated with poorer iron status and more fever in children <30 mo of age. In children aged <30 mo, the negative effects of malaria parasitemia on iron status were seen with any parasitemia. However, in children aged ≥30 mo, the negative effects were only seen in children with >5000 parasites/ $\mu$ L of blood (24). The age differences seen in the relationships between malaria parasitemia and iron status indicators and fever indicate that if malaria impacts child development through the pathways mentioned above, these relationships are likely to change with age. It is therefore important that future studies examine the relationship between malaria infection and child development in infants and young children and examine how this relationship differs by intensity and frequency of infection.

The negative relationship between malaria infection and motor activity in young children has not been reported previously. In addition, the large sample size and the natural setting in which the continuous direct observations were conducted adds considerably to the current literature on health, nutrition, and motor activity. Anemia, stunting, and malaria affect millions of children worldwide and amelioration of these problems has the

potential to improve both the health of affected children and their motor, cognitive, and social-emotional development.

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